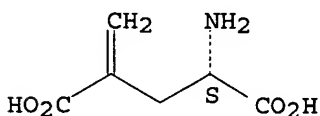


=> s 4-methylene-l-glutamic acid/cn
L1 1 4-METHYLENE-L-GLUTAMIC ACID/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 16804-57-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, 4-methylene-, L- (8CI)
OTHER NAMES:
CN γ -Methylene-L-glutamic acid
CN γ -Methyleneglutamic acid
CN 4-Methylene-L-glutamic acid
CN 4-Methyleneglutamic acid
CN L- γ -Methyleneglutamate
CN L-4-Methyleneglutamic acid
FS STEREOSEARCH
MF C6 H9 N O4
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS,
CASREACT, CHEMINFORMRX, EMBASE, IPA, NAPRALERT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

78 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
78 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 6.87 | 7.53 |

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FILE LAST UPDATED: 17 Aug 2005 (20050817/ED)

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substance identification.

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 78 16804-57-2
 3344682 PREP/RL
 L2 10 16804-57-2/PREP
 (16804-57-2 (L) PREP/RL)

=> s 16804-57-2/proc
 78 16804-57-2
 3732873 PROC/RL
 L3 5 16804-57-2/PROC
 (16804-57-2 (L) PROC/RL)

=> s 16804-57-2/pur
 78 16804-57-2
 216443 PUR/RL
 L4 0 16804-57-2/PUR
 (16804-57-2 (L) PUR/RL)

=> s 12 or 13
 L5 15 L2 OR L3

=> s 15 and pyrogluta?
 4244 PYROGLUTA?
 L6 3 L5 AND PYROGLUTA?

=> d 1-3 ibib abs hitstr

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:392435 CAPLUS
 DOCUMENT NUMBER: 140:375488
 TITLE: Process for synthesizing L-methyleneglutamic acid and
 analogs
 INVENTOR(S): Kochat, Harry; Chen, Xinghai; Wu, Ye; Huang, Qiuli;
 Wang, Jianyan; Gerusz, Vincent
 PATENT ASSIGNEE(S): Bionumerik Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 13 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2004039314 | A2 | 20040513 | WO 2003-US33236 | 20031022 |
| WO 2004039314 | A3 | 20041209 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | |
| US 2004106826 | A1 | 20040603 | US 2003-627484 | 20030725 |
| CA 2503029 | AA | 20040513 | CA 2003-2503029 | 20031022 |
| EP 1554235 | A2 | 20050720 | EP 2003-781352 | 20031022 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| PRIORITY APPLN. INFO.: | | | US 2002-421489P | P 20021025 |
| | | | US 2003-627484 | A 20030725 |
| | | | WO 2003-US33236 | W 20031022 |

OTHER SOURCE(S): CASREACT 140:375488

AB A process for synthesizing 4-methylene-L-glutamic acid and analogs comprises converting (2S)-pyroglutamic acid or a derivative to a 4-enamine derivative, hydrolysis to a 4-hydroxymethylene derivative, reduction to a 4-methylene derivative, and treatment with strong base to effect ring

cleavage. In the examples, L-pyroglutamic acid was C/N-protected and reacted with DMF diisopropyl acetal to form intermediate Et 4-[(dimethylamino)methylene]-N-(tert-butoxycarbonyl)-L-pyroglutamate, which was converted into 4-methylene-L-glutamic acid hydrochloride.

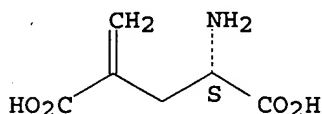
IT 16804-57-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(process for synthesizing L-methyleneglutamic acid and analogs)

RN 16804-57-2 CAPLUS

CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:631298 CAPLUS

DOCUMENT NUMBER: 121:231298

TITLE: Efficient synthesis of 4-methylene-L-glutamic acid and its cyclopropyl analog

AUTHOR(S): Ezquerra, Jesus; Pedregal, Concepcion; Mico, Irene; Najera, Carmen

CORPORATE SOURCE: Cent. Invest. Lilly S. A., Valdeolmos, 28130, Spain

SOURCE: Tetrahedron: Asymmetry (1994), 5(5), 921-6

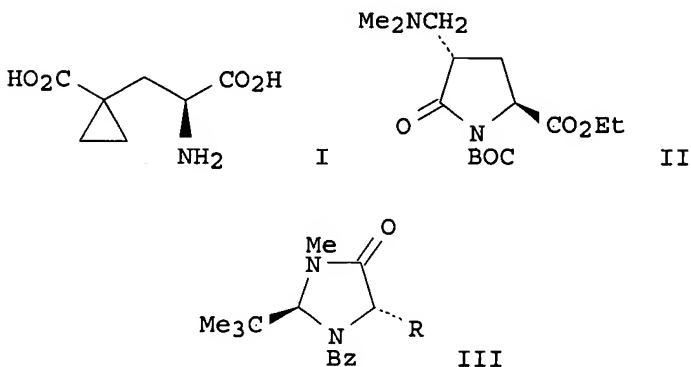
CODEN: TASYE3; ISSN: 0957-4166

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 121:231298

GI



AB Title compds. L-NHCH(CO2H)CH2C(CO2H):CH2 and cyclopropyl analog I were obtained from protected pyroglutamate Boc-pGlu-OEt (Boc = Me3CO2C) in 2 and 3 steps, resp. Key methylenepyroglutamate intermediate II was prepared by reaction of the protected pyroglutamate lithium lactam enolate with Eschenmoser's salt. Cyclopropyl derivative I was also prepared from imidazolidone III (R = H) in 3 steps. The intermediate III [R = CH2C(CO2Bu):CH2] was obtained by diastereoselective reaction of the lithium enolate of III (R = H) with Bu (2-tosylmethyl)acrylate.

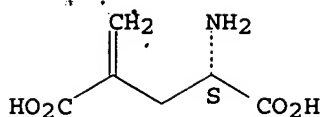
IT 16804-57-2P, 4-Methylene-L-glutamic acid

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, from pyroglutamic acid)

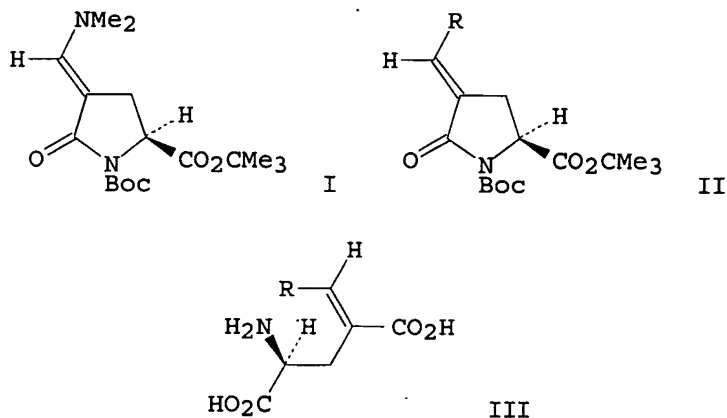
RN 16804-57-2 CAPLUS

CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

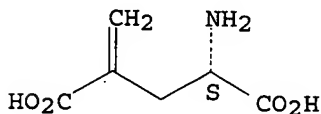


L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1993:671664 CAPLUS
 DOCUMENT NUMBER: 119:271664
 TITLE: Synthesis of naturally occurring 4-alkylideneglutamic acids
 AUTHOR(S): Moody, Claire M.; Young, Douglas W.
 CORPORATE SOURCE: Sch. Chem. Mol. Sci., Univ. Sussex, Falmer/Brighton, BN1 9QJ, UK
 SOURCE: Tetrahedron Letters (1993), 34(29), 4667-70
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 119:271664
 GI



AB Enaminone I (Boc = Me₃CO₂C) reacted with Grignard reagents RMgBr (R = Me, Et, Ph, C.tplbond.CH) to afford (E)-alkylidene derivs. II. II (R = H, Me, Et) were converted to 4-alkylideneglutamic acids III (R = H, Me, Et).
 IT 16804-57-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 16804-57-2 CAPLUS
 CN L-Glutamic acid, 4-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



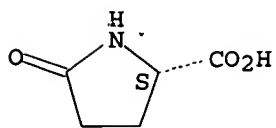
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s pyroglutamic acid/cn
L7 1 PYROGLUTAMIC ACID/CN

=> d

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 98-79-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Proline, 5-oxo- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Proline, 5-oxo-, L- (8CI)
OTHER NAMES:
CN (-)-2-Pyrrolidone-5-carboxylic acid
CN (-)-Pyroglutamic acid
CN (2S)-5-Oxopyrrolidine-2-carboxylic acid
CN (5S)-2-Oxopyrrolidine-5-carboxylic acid
CN (S)-(-)- γ -Butyrolactam- γ -carboxylic acid
CN (S)-(-)-2-Pyrrolidone-5-carboxylic acid
CN (S)-2-Pyrrolidone-5-carboxylic acid
CN (S)-5-Oxo-2-pyrrolidinecarboxylic acid
CN (S)-Pyroglutamic acid
CN 2-L-Pyrrolidone-5-carboxylic acid
CN 2-Oxopyrrolidine-5(S)-carboxylic acid
CN 2-Pyrrolidinone-5-carboxylic acid
CN 5-Carboxy-2-pyrrolidinone
CN 5-Oxo-L-proline
CN 5-Oxoproline
CN 5-Pyrrolidinone-2-carboxylic acid
CN Ajidew A 100
CN Glutimic acid
CN Glutiminic acid
CN L-2-Pyrrolidone-5-carboxylic acid
CN L-5-Carboxy-2-pyrrolidinone
CN L-5-Oxo-2-pyrrolidinecarboxylic acid
CN L-5-Oxoproline
CN L-Glutamic acid, γ -lactam
CN L-Glutimic acid
CN L-Glutiminic acid
CN L-Pyroglutamic acid
CN L-Pyrrolidinonecarboxylic acid
CN L-Pyrrolidonecarboxylic acid
CN NSC 143034
CN Oxoproline
CN Oxopyrrolidinecarboxylic acid
CN PCA
CN Pidolic acid
CN Pidolidone
CN **Pyroglutamic acid**
CN Pyrrolidinonecarboxylic acid
CN Pyrrolidone-5-carboxylic acid
CN Pyrrolidonecarboxylic acid
AR 35255-51-7
FS STEREOSEARCH
DR 6886-28-8, 498-91-9, 16891-48-8, 87430-62-4, 29222-42-2, 312618-42-1
MF C5 H7 N O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, GMELIN*,
HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC,
PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2,
USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2694 REFERENCES IN FILE CA (1907 TO DATE)
178 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2700 REFERENCES IN FILE CAPLUS (1907 TO DATE)
20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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